

Claims:

1. A mammalian immune cell exhibiting a targeted endogenous gene-specific knockout phenotype, said immune cell altering an immune response in a mammal via the modulation of T cell activity.
2. The immune cell of claim 1, wherein said cell comprises a construct that inhibits the expression of said endogenous target gene.
3. The immune cell of claim 2, wherein said construct is selected from the group consisting of siRNA and hybrid DNA/RNA.
4. The immune cell of claim 1, 2 or 3, wherein said endogenous gene encodes a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor.
5. The immune cell of any one of claims 1 to 4, wherein said immune cell is selected from the group consisting of an endothelial cell and an antigen presenting cell.
6. The immune cell of claim 5, wherein said antigen presenting cell is selected from the group consisting of a dendritic cell, a macrophage, a myeloid cell, a B lymphocyte and mixtures thereof.
7. The immune cell of claim 6, wherein said immune cell is a dendritic cell.
8. The immune cell of claim 7, wherein said dendritic cell is activated.
9. The immune cell of any one of claims 1 to 7, wherein said siRNA or hybrid DNA/RNA is provided within a plasmid or vector.

10. The immune cell of claim 9, wherein said plasmid or vector additionally comprises an expressible nucleic acid sequence encoding an antigen.

5 11. The immune cell of claim 8 or 9, wherein said dendritic cell additionally comprises tumor cell mRNA.

12. The immune cell of claim 4 or 5, wherein said surface marker, chemokine, cytokine, enzyme or transcription factor is selected from the group  
10 consisting of  $\text{TNF}\alpha$ , IL-1, IL-1b, IL-2,  $\text{TNF}\beta$ , IL-6, IL-7, IL-8, IL-23, IL-15, IL18, IL-12,  $\text{IFN}\gamma$ ,  $\text{IFN}\alpha$ , lymphotoxin, DEC-25, CD11c, CD40, CD80, CD86, MHC1, MHCII, ICAM-1, TRANCE, CD200, CD200 receptor, CD83, CD2, CD44, CD91, TLR-4, TLR-9, 4-1BBL, nicotinic receptor, GITR-L, OX-40L, CD-CK1, TARC/CCL17, CCL3, CCL4, CXCL9, CXCL10, IKK- $\beta$ , NF- $\kappa$ B, STAT4,  
15 ICSBP/ $\text{IFN}$ , regulatory factor 8, TRAIL, Inos, arginase, Fc $\gamma$ RI and II, thrombin, MIP-1 $\alpha$  and MIP-1B.

13. The immune cell of claim 12, wherein said cytokine is selected from IL-12 and  $\text{TNF}\alpha$ .

20 14. The immune cell of claim 12 or 13, wherein said immune cell inhibits T cell activity.

15. The immune cell of claim 4 or 5, wherein said surface marker and enzyme are selected from the group consisting of B7-H1, EP2, IL-10 receptor, VEGF-receptor, CD101, PD-L1, PD-L2, HLA-11, DEC-205, CD36 and indoleamine 2,3-dioxygenase.

16. The immune cell of claim 15, wherein said immune cell  
30 stimulates T cell activity.

17. The immune cell of claim 14 or 16, wherein said immune cell is administered to a mammalian subject for the treatment of an immune disorder.

5 18. The immune cell of claim 17, wherein said immune disorder is selected from the group consisting of septic shock, rheumatoid arthritis, transplant rejection, scleroderma, immune mediated diabetes, chronic inflammatory bowel syndrome, HIV, cancer, colitis, Crohn's disease, Goodpasture's syndrome, Multiple Sclerosis, Grave's disease, Hashimoto's  
10 thyroiditis, Autoimmune pernicious anemia, Autoimmune Addison's disease, Vitiligo, Myasthenia gravis, Scleroderma, Systemic lupus erythematosus, Primary Sjogren's syndrome, Polymyositis, Pemphigus vulgaris, Ankylosing spondylitis, Acute anterior uveitis, Hypoglycemia and inflammation associated with chronic illness.

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19. The immune cell of any one of claims 1 to 18, wherein said immune cell is provided as a composition comprising a pharmaceutically acceptable carrier.

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20. The immune cell of claim 19, wherein said composition additionally comprises an adjuvant and/or an antigen.

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21. The use of a mammalian immune cell that exhibits a targeted gene-specific knockout phenotype, wherein said gene is selected from one or  
more of a surface marker, a chemokine, a cytokine, an enzyme and a transcriptional factor, in a medicament for the treatment of an immune disorder characterized by inappropriate T cell activity.

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22. The use of a siRNA possessing specific homology to part or the entire exon region of a gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor of an antigen presenting cell (APC), in a medicament for the treatment of an immune disorder characterized by inappropriate T cell activity.

23. The use of claim 20 or 21, wherein said gene is selected from the group consisting of  $\text{TNF}\alpha$ , IL-1, IL-1b, IL-2,  $\text{TNF}\beta$ , IL-6, IL-7, IL-8, IL-23, IL-15, IL18, IL-12,  $\text{IFN}\gamma$ ,  $\text{IFN}\alpha$ , lymphotoxin, DEC-25, CD11c, CD40, CD80, CD86, MHC I, MHC II, ICAM-1, TRANCE, CD200, CD200 receptor, CD83,  
5 CD2, CD44, CD91, TLR-4, TLR-9, 4-1BBL, nicotinic receptor, GITR-L, OX-40L, CD-CK1, TARC/CCL17, CCL3, CCL4, CXCL9, CXCL10,  $\text{IKK-}\beta$ ,  $\text{NF-}\kappa\text{B}$ , STAT4, ICSBP/ $\text{IFN}$ , regulatory factor 8, TRAIL, Inos, arginase, Fc $\gamma$ RI and II, thrombin, MIP-1 $\alpha$  and MIP-1B.

10 24. The use of claim 22, wherein said T cell activity is inhibited.

25. The use of claim 20 or 21, wherein said gene is selected from the group consisting of B7-H1, EP2, IL-10 receptor, VEGF-receptor, CD101, PD-L1, PD-L2, HLA-11, DEC-205, CD36 and indoleamine 2,3-dioxygenase.

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26. The use of claim 25, wherein said T cell activity is stimulated.

27. The use of claim 23 or 24, wherein said immune disorder is selected from the group consisting of septic shock, rheumatoid arthritis, transplant rejection, scleroderma, immune mediated diabetes, chronic  
20 inflammatory bowel syndrome, HIV, cancer, colitis, Crohn's disease, Goodpasture's syndrome, Multiple Sclerosis, Grave's disease, Hashimoto's thyroiditis, Autoimmune pernicious anemia, Autoimmune Addison's disease, Vitiligo, Myasthenia gravis, Scleroderma, Systemic lupus erythematosus, Primary Sjogren's syndrome, Polymyositis, Pemphigus vulgaris, Ankylosing  
25 spondylitis, Acute anterior uveitis, Hypoglycemia and inflammation associated with chronic illness..

28. The use of any one of claims 21 to 27, wherein said immune cell  
30 is selected from an endothelial cell and an antigen presenting cell (APC).

29. The use of claim 28, wherein said antigen presenting cell is selected from the group consisting of a dendritic cell, a macrophage, a myeloid cell, a B lymphocyte and mixtures thereof.

5 30. The use of claim 29, wherein said immune cell is a dendritic cell.

31. The use of claim 30, wherein said dendritic cell is activated.

32. A composition for the treatment of an immune disorder, said  
10 composition comprising at least one of:

(a) a construct that inhibits the expression of an endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor in an immune cell such that said immune cell alters T cell activity; and

15 (b) an immune cell wherein said immune cell comprises at least one construct that inhibits the expression of an endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor;; and

(c) a pharmaceutically acceptable carrier,  
20 wherein said composition alters T cell activity leading to an altered immune response.

33. The composition of claim 32, wherein said construct is selected from the group consisting of siRNA and hybrid DNA/RNA.

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34. The composition of claim 32 or 33, wherein said immune cell is selected from the group consisting of an endothelial cell and an antigen presenting cell.

30 35. The composition of claim 34, wherein said antigen presenting cell is selected from the group consisting of a dendritic cell, a macrophage, a myeloid cell, a B lymphocyte and mixtures thereof.

36. The composition of claim 35, wherein said immune cell is a dendritic cell.

37. The composition of claim 36, wherein said dendritic cell is  
5 activated.

38. The composition of claim 33, wherein said siRNA or hybrid DNA/RNA is provided within a plasmid or vector.

10 39. The composition of claim 38, wherein said plasmid or vector additionally comprises an expressible nucleic acid sequence encoding an antigen.

40. The composition of claim 35 or 36, wherein said dendritic cell  
15 additionally comprises tumor cell mRNA.

41. The composition of any one of claims 32 to 40, wherein said surface marker, chemokine, cytokine, enzyme or transcription factor is selected from the group consisting of  $\text{TNF}\alpha$ , IL-1, IL-1b, IL-2,  $\text{TNF}\beta$ , IL-6, IL-7, IL-8, IL-23, IL-15, IL18, IL-12,  $\text{IFN}\gamma$ ,  $\text{IFN}\alpha$ , lymphotoxin, DEC-25, CD11c,  
20 CD40, CD80, CD86, MHC I, MHC II, ICAM-1, TRANCE, CD200, CD200 receptor, CD83, CD2, CD44, CD91, TLR-4, TLR-9, 4-1BBL, nicotinic receptor, GTR-L, OX-40L, CD-CK1, TARC/CCL17, CCL3, CCL4, CXCL9, CXCL10, IKK- $\beta$ , NF- $\kappa$ B, STAT4, ICSBP/IFN, regulatory factor 8, TRAIL, Inos, arginase,  
25 Fc $\gamma$ RI and II, thrombin, MIP-1 $\alpha$  and MIP-1B.

42. The composition of claim 41, wherein said cytokine is selected from IL-12 and  $\text{TNF}\alpha$ .

30 43. The composition of any one of claims 32 to 40, wherein said surface marker and enzyme are selected from the group consisting of B7-H1, EP2, IL-10 receptor, VEGF-receptor, CD101, PD-L1, PD-L2, HLA-11, DEC-205, CD36 and indoleamine 2,3-dioxygenase.

44. The composition of any one of claims 32 to 43, wherein said immune disorder is selected from the group consisting of septic shock, rheumatoid arthritis, transplant rejection, scleroderma, immune mediated  
5 diabetes, chronic inflammatory bowel syndrome, HIV, cancer, colitis, Crohn's disease, Goodpasture's syndrome, Multiple Sclerosis, Grave's disease, Hashimoto's thyroiditis, Autoimmune pernicious anemia, Autoimmune Addison's disease, Vitiligo, Myasthenia gravis, Scleroderma, Systemic lupus erythematosus, Primary Sjogren's syndrome, Polymyositis, Pemphigus  
10 vulgaris, Ankylosing spondylitis, Acute anterior uveitis, Hypoglycemia and inflammation associated with chronic illness.

45. The composition of any one of claims 32 to 44, wherein said composition is used to perfuse tissues and/or organs *ex vivo*.

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46. A method for inhibiting the T cell activating ability of a DC, the method comprising transforming said DC with a construct capable of inhibiting the expression of an endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor.

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47. A method for decreasing the immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing said organ with a composition that suppresses T cell activity, said composition comprising at least one construct that inhibits the expression of an  
25 endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor and a pharmaceutically acceptable carrier.

48. The method of claim 46 or 47, wherein said construct is selected  
30 from siRNA and hybrid DNA/RNA.

49. The method of claim 48, wherein said siRNA is provided within an antigen presenting immune cell.

50. A method for making an immune cell that alters the activity of T cells *in vivo*, said method comprising;

- transforming immune cells *in vitro* with at least one construct that inhibits the expression of an endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor.

51. A method for the treatment of autoimmune disorders and transplantation rejection in a mammalian subject, said method comprising administering a therapeutically effective amount of a composition to said subject, said composition comprising DC that contain at least one construct that inhibits the expression of an endogenous target gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor, wherein said DC suppresses T cell activity.

52. The method of claim 50 or 51, wherein said construct is selected from siRNA and hybrid DNA/RNA.

53. A method for the treatment of autoimmune disorders and transplantation rejection in a mammalian subject, said method comprising administering a therapeutically effective amount of a composition to said subject, said composition comprising an siRNA targeted to inhibit expression of an endogenous target gene in an antigen presenting cell, said gene encoding a surface marker, a chemokine, a cytokine, an enzyme or a transcriptional factor, wherein said siRNA suppresses T cell activity.

54. The method of claims 51, 52 or 53, wherein said autoimmune disorder is selected from the group consisting of septic shock, rheumatoid arthritis, transplant rejection, scleroderma, immune mediated diabetes, chronic inflammatory bowel syndrome, HIV, cancer, colitis, Crohn's disease, Goodpasture's syndrome, Multiple Sclerosis, Grave's disease, Hashimoto's thyroiditis, Autoimmune pernicious anemia, Autoimmune Addison's disease, Vitiligo, Myasthenia gravis, Scleroderma, Systemic lupus erythematosus, Primary Sjogren's syndrome, Polymyositis, Pemphigus vulgaris, Ankylosing



spondylitis, Acute anterior uveitis, Hypoglycemia and inflammation associated with chronic illness.